

THE LANCET

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed.
We post it as supplied by the authors.

Supplement to: Flaxman A, Marchevsky NG, Jenkin D, et al. Reactogenicity and immunogenicity after a late second dose or a third dose of ChAdOx1 nCoV-19 in the UK: a substudy of two randomised controlled trials (COV001 and COV002). *Lancet* 2021; published online Sept 1. [http://dx.doi.org/10.1016/S0140-6736\(21\)01699-8](http://dx.doi.org/10.1016/S0140-6736(21)01699-8).

Supplementary Methods

MSD multi-plex immunoassay

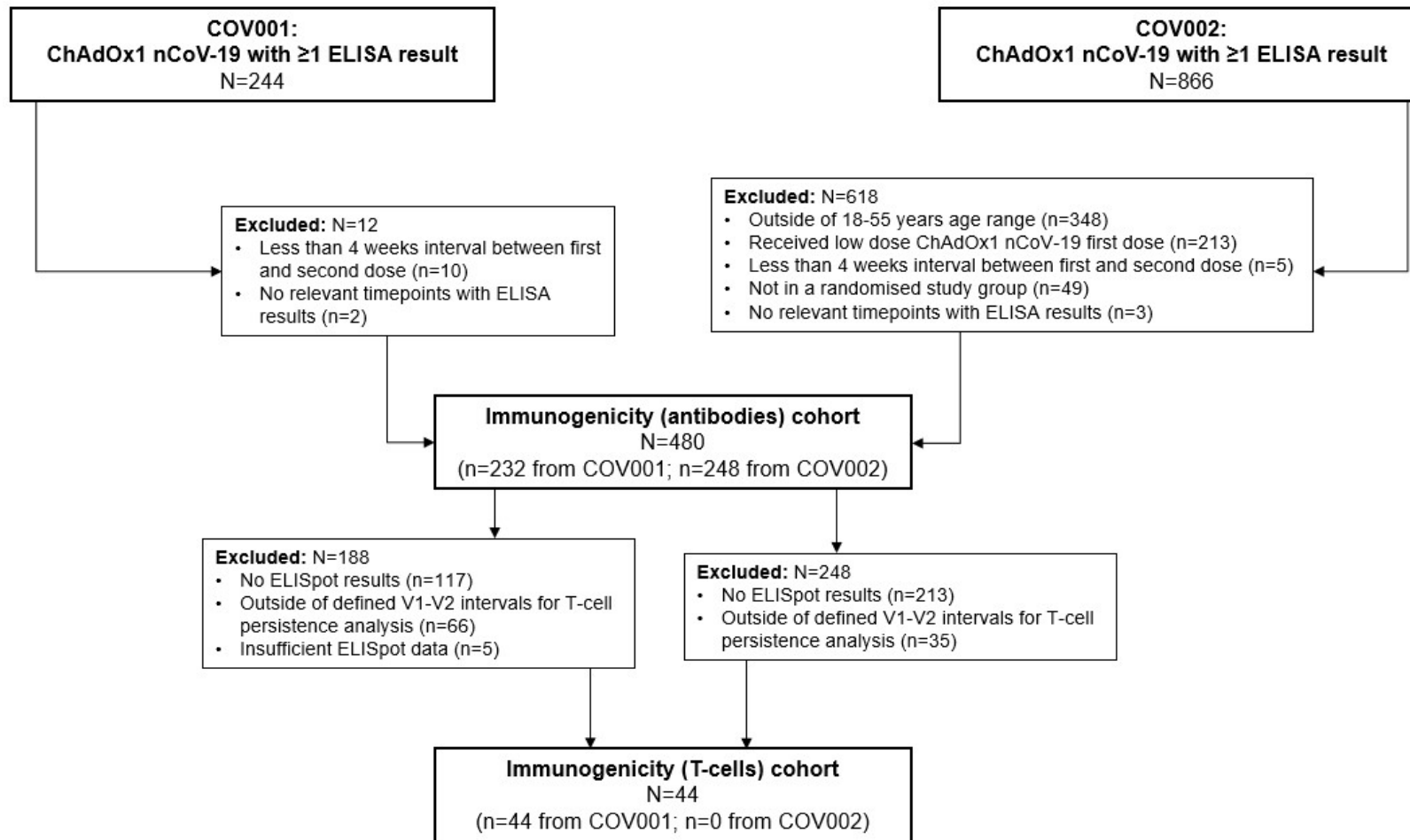
V-PLEX SARS-CoV-2 Panel 6 (IgG) kits were used following manufacturer's instructions (Meso Scale Discovery, K15433U) Briefly, plates pre-coated with a panel of 7 SARS-CoV-2 WT and variant antigens were blocked for 30 minutes at room temperature with shaking (600rpm) and washed 3x with PBS-T. Reference calibrator and three internal controls provided in the kit were diluted as instructed and test sera were diluted 1:2000 and plated in duplicate. Plates were incubated as above for 2 hours, and then washed 3x with PBS-T. Wells were then incubated in the dark as above with SULFO-TAG Anti-human IgG for 1 hour. Plates were washed 3x with PBS-T followed by a final wash with PBS and read within 5 minutes of the addition of read buffer on a MESO QuickPlex SQ 120MM plate reader with Methodical Mind TM 2.0.15 software. Data was exported and analysed using MSD Discovery Workbench v4.0 ensuring the following QC criteria were met: sample CVs < 20%; the IC calculated concentration was within 70-130% of expected concentration; and the reference standard percentage recovery was within 80-120%. Samples with signals above the detection limit of the assay were repeated at a higher dilution to ensure that the signal fell within the detection range of the assay.

Delta Variant ELISA

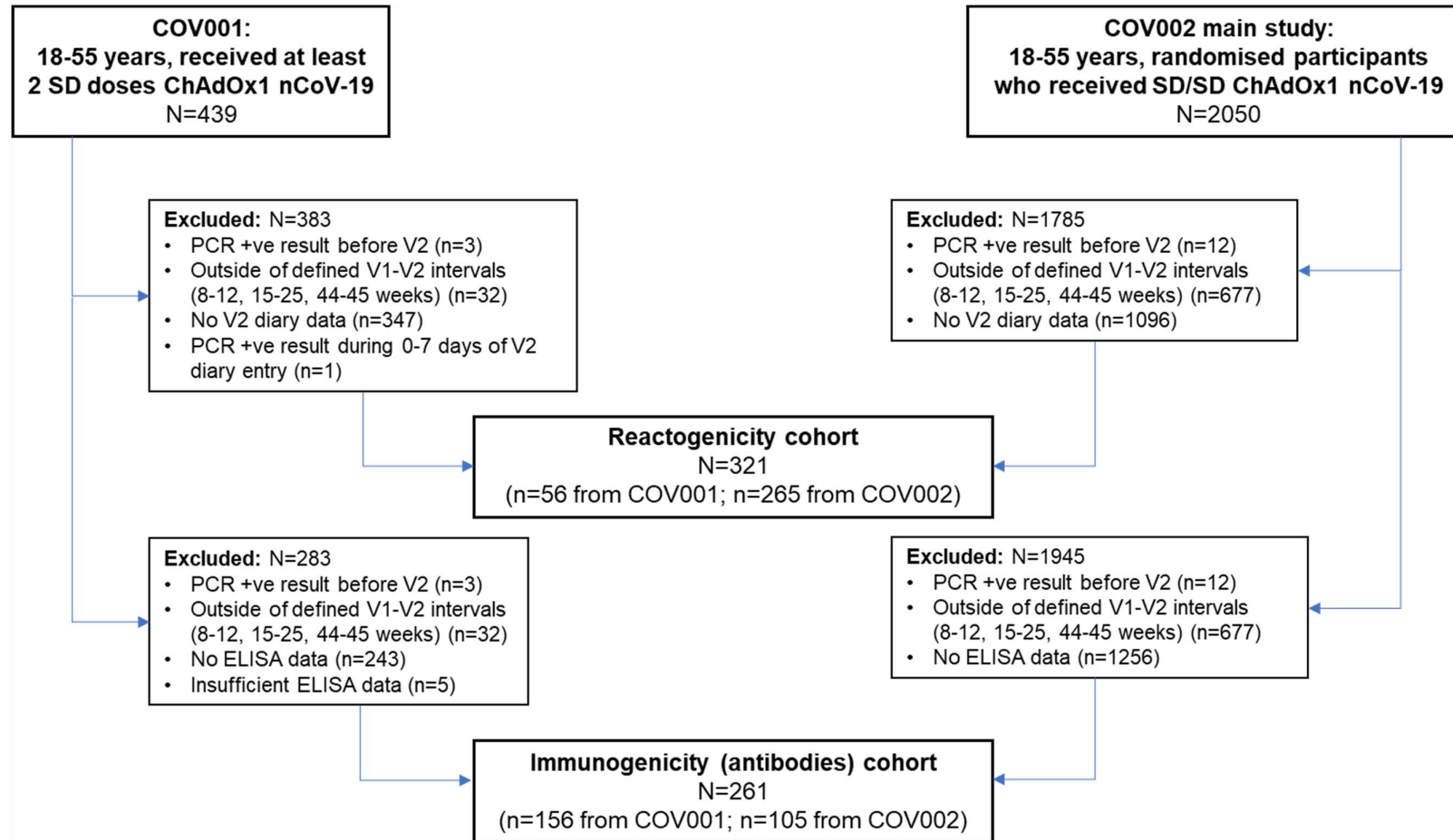
To measure antibody responses to Delta variant (B.1.617.2) the ELISA assay as previously described¹ was adapted to coat with 2.0ug/ml of SARS-CoV-2 spike protein from Delta variant, provided by AstraZeneca.

Supplementary Figures

Supplementary Figure 1 – CONSORT flow diagram for single dose persistence cohorts



Supplementary Figure 2 – CONSORT flow diagram for two dose cohorts. SD = standard dose.



Supplementary Tables

Supplementary Table 1- Baseline characteristics of the single dose persistence cohort

	Immunogenicity: antibodies	Immunogenicity: T- cells
Number of participants	480	44
Sex (female)	237 (49.4%)	19 (43.2%)
Age (median [IQR])	37.2 [29.0, 47.0]	31.0 [24.1, 40.4]
<i>18-29 years</i>	133 (27.7%)	18 (40.9%)
<i>30-39 years</i>	136 (28.3%)	14 (31.8%)
<i>40-55 years</i>	211 (44.0%)	12 (27.3%)
BMI (median [IQR])	24.9 [22.4, 27.8]	23.7 [21.8, 25.8]
Ethnicity:		
<i>White</i>	435 (90.6%)	40 (90.9%)
<i>Black</i>	5 (1.0%)	0 (0.0%)
<i>Asian</i>	23 (4.8%)	1 (2.3%)
<i>Other</i>	17 (3.5%)	3 (6.8%)
<i>Missing</i>	0 (0.0%)	0 (0.0%)

Supplementary Table 1 - Baseline characteristics of the two dose cohort

	Reactogenicity			Immunogenicity: antibodies		
	All	COV001	COV002	All	COV001	COV002
Number of participants	321	56	265	261	156	105
Sex (female)	204 (63.6%)	31 (55.4%)	173 (65.3%)	124 (47.5%)	67 (42.9%)	57 (54.3%)
Age (median [IQR])	41.0 [30.2, 49.0]	33.5 [26.4, 44.1]	42.0 [32.0, 49.3]	37.2 [29.4, 46.0]	35.0 [29.4, 43.7]	39.0 [30.0, 50.0]
18-29 years	74 (23.1%)	17 (30.4%)	57 (21.5%)	68 (26.1%)	42 (26.9%)	26 (24.8%)
30-39 years	74 (23.1%)	18 (32.1%)	56 (21.1%)	82 (31.4%)	55 (35.3%)	27 (25.7%)
40-55 years	173 (53.9%)	21 (37.5%)	152 (57.4%)	111 (42.5%)	59 (37.8%)	52 (49.5%)
BMI (median [IQR])	24.8 [22.4, 28.2]	23.8 [21.3, 26.3]	25.1 [22.8, 28.4]	24.5 [22.2, 27.3]	24.0 [22.2, 26.8]	24.9 [22.1, 27.7]
Ethnicity:						
White	299 (93.1%)	51 (91.1%)	248 (93.6%)	238 (91.2%)	141 (90.4%)	97 (92.4%)
Black	1 (0.3%)	1 (1.8%)	0 (0.0%)	3 (1.1%)	3 (1.9%)	0 (0.0%)
Asian	14 (4.4%)	0 (0.0%)	14 (5.3%)	10 (3.8%)	4 (2.6%)	6 (5.7%)
Other	7 (2.2%)	4 (7.1%)	3 (1.1%)	10 (3.8%)	8 (5.1%)	2 (1.9%)
Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
V1-V2 interval:						
<8 weeks	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
8-12 weeks	267 (83.2%)	20 (35.7%)	247 (93.2%)	115 (44.1%)	20 (12.8%)	95 (90.5%)
15-25 weeks	24 (7.5%)	6 (10.7%)	18 (6.8%)	116 (44.4%)	106 (67.9%)	10 (9.5%)
44-45 weeks	30 (9.3%)	30 (53.6%)	0 (0.0%)	30 (11.5%)	30 (19.2%)	0 (0.0%)

Supplementary Table 2 - Baseline characteristics of the third dose cohort

	Reactogenicity	Immunogenicity: antibodies	Immunogenicity: T-cells
Number of participants	80	75	15
Sex (female)	32 (40.0%)	29 (38.7%)	10 (66.7%)
Age (median [IQR])	37.0 [30.6, 41.9]	37.2 [30.8, 42.2]	39.5 [32.1, 44.2]
18-29 years	16 (20.0%)	14 (18.7%)	3 (20.0%)
30-39 years	36 (45.0%)	33 (44.0%)	5 (33.3%)
40-55 years	28 (35.0%)	28 (37.3%)	7 (46.7%)
BMI (median [IQR])	24.0 [22.5, 26.7]	24.0 [22.6, 26.8]	23.9 [22.0, 29.2]
Ethnicity:			
White	71 (88.8%)	67 (89.3%)	14 (93.3%)
Black	1 (1.2%)	1 (1.3%)	1 (6.7%)
Asian	3 (3.8%)	2 (2.7%)	0 (0.0%)
Other	5 (6.2%)	5 (6.7%)	0 (0.0%)
Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)
V1-V2 interval:			
<8 weeks	0 (0.0%)	0 (0.0%)	0 (0.0%)
8-12 weeks	15 (18.8%)	15 (20.0%)	15 (100.0%)
15-25 weeks	65 (81.2%)	60 (80.0%)	0 (0.0%)
44-45 weeks	0 (0.0%)	0 (0.0%)	0 (0.0%)

Supplementary Table 4 - Local and solicited adverse reactions in the first 7 days after the second dose of vaccine for the two dose cohort

Symptom	V1-V2 Interval	None	Mild	Moderate	Severe	Potentially life threatening/hospitalisation	Any
Pain	8-12 weeks	170/267 (64%, 58%-69%)	96/267 (36%, 30%-42%)	1/267 (0%, 0%-2%)	0/267 (0%, 0%-1%)	0/267 (0%, 0%-1%)	97/267 (36%, 31%-42%)
	15-25 weeks	13/24 (54%, 33%-74%)	9/24 (38%, 19%-59%)	2/24 (8%, 1%-27%)	0/24 (0%, 0%-14%)	0/24 (0%, 0%-14%)	11/24 (46%, 26%-67%)
	44-45 weeks	18/30 (60%, 41%-77%)	9/30 (30%, 15%-49%)	3/30 (10%, 2%-27%)	0/30 (0%, 0%-12%)	0/30 (0%, 0%-12%)	12/30 (40%, 23%-59%)
Redness	8-12 weeks	266/267 (100%, 98%-100%)	1/267 (0%, 0%-2%)	0/267 (0%, 0%-1%)	0/267 (0%, 0%-1%)	0/267 (0%, 0%-1%)	1/267 (0%, 0%-2%)
	15-25 weeks	24/24 (100%, 86%-100%)	0/24 (0%, 0%-14%)	0/24 (0%, 0%-14%)	0/24 (0%, 0%-14%)	0/24 (0%, 0%-14%)	0/24 (0%, 0%-14%)
	44-45 weeks	30/30 (100%, 88%-100%)	0/30 (0%, 0%-12%)	0/30 (0%, 0%-12%)	0/30 (0%, 0%-12%)	0/30 (0%, 0%-12%)	0/30 (0%, 0%-12%)
Warmth	8-12 weeks	234/267 (88%, 83%-91%)	32/267 (12%, 8%-16%)	1/267 (0%, 0%-2%)	0/267 (0%, 0%-1%)	0/267 (0%, 0%-1%)	33/267 (12%, 9%-17%)
	15-25 weeks	21/24 (88%, 68%-97%)	3/24 (12%, 3%-32%)	0/24 (0%, 0%-14%)	0/24 (0%, 0%-14%)	0/24 (0%, 0%-14%)	3/24 (12%, 3%-32%)
	44-45 weeks	25/30 (83%, 65%-94%)	5/30 (17%, 6%-35%)	0/30 (0%, 0%-12%)	0/30 (0%, 0%-12%)	0/30 (0%, 0%-12%)	5/30 (17%, 6%-35%)
Itch	8-12 weeks	255/267 (96%, 92%-98%)	12/267 (4%, 2%-8%)	0/267 (0%, 0%-1%)	0/267 (0%, 0%-1%)	0/267 (0%, 0%-1%)	12/267 (4%, 2%-8%)
	15-25 weeks	23/24 (96%, 79%-100%)	1/24 (4%, 0%-21%)	0/24 (0%, 0%-14%)	0/24 (0%, 0%-14%)	0/24 (0%, 0%-14%)	1/24 (4%, 0%-21%)
	44-45 weeks	29/30 (97%, 83%-100%)	1/30 (3%, 0%-17%)	0/30 (0%, 0%-12%)	0/30 (0%, 0%-12%)	0/30 (0%, 0%-12%)	1/30 (3%, 0%-17%)
Swelling	8-12 weeks	267/267 (100%, 99%-100%)	0/267 (0%, 0%-1%)	0/267 (0%, 0%-1%)	0/267 (0%, 0%-1%)	0/267 (0%, 0%-1%)	0/267 (0%, 0%-1%)
	15-25 weeks	23/24 (96%, 79%-100%)	1/24 (4%, 0%-21%)	0/24 (0%, 0%-14%)	0/24 (0%, 0%-14%)	0/24 (0%, 0%-14%)	1/24 (4%, 0%-21%)
	44-45 weeks	30/30 (100%, 88%-100%)	0/30 (0%, 0%-12%)	0/30 (0%, 0%-12%)	0/30 (0%, 0%-12%)	0/30 (0%, 0%-12%)	0/30 (0%, 0%-12%)
Induration	8-12 weeks	266/267 (100%, 98%-100%)	1/267 (0%, 0%-2%)	0/267 (0%, 0%-1%)	0/267 (0%, 0%-1%)	0/267 (0%, 0%-1%)	1/267 (0%, 0%-2%)
	15-25 weeks	24/24 (100%, 86%-100%)	0/24 (0%, 0%-14%)	0/24 (0%, 0%-14%)	0/24 (0%, 0%-14%)	0/24 (0%, 0%-14%)	0/24 (0%, 0%-14%)
	44-45 weeks	30/30 (100%, 88%-100%)	0/30 (0%, 0%-12%)	0/30 (0%, 0%-12%)	0/30 (0%, 0%-12%)	0/30 (0%, 0%-12%)	0/30 (0%, 0%-12%)
Tenderness	8-12 weeks	81/267 (30%, 25%-36%)	181/267 (68%, 62%-73%)	5/267 (2%, 1%-4%)	0/267 (0%, 0%-1%)	0/267 (0%, 0%-1%)	186/267 (70%, 64%-75%)
	15-25 weeks	10/24 (42%, 22%-63%)	12/24 (50%, 29%-71%)	2/24 (8%, 1%-27%)	0/24 (0%, 0%-14%)	0/24 (0%, 0%-14%)	14/24 (58%, 37%-78%)

Symptom	V1-V2 Interval	None	Mild	Moderate	Severe	Potentially life threatening/hospitalisation	Any
	44-45 weeks	9/30 (30%, 15%-49%)	17/30 (57%, 37%-75%)	4/30 (13%, 4%-31%)	0/30 (0%, 0%-12%)	0/30 (0%, 0%-12%)	21/30 (70%, 51%-85%)
Feverish	8-12 weeks	232/267 (87%, 82%-91%)	25/267 (9%, 6%-14%)	8/267 (3%, 1%-6%)	2/267 (1%, 0%-3%)	0/267 (0%, 0%-1%)	35/267 (13%, 9%-18%)
	15-25 weeks	21/24 (88%, 68%-97%)	1/24 (4%, 0%-21%)	2/24 (8%, 1%-27%)	0/24 (0%, 0%-14%)	0/24 (0%, 0%-14%)	3/24 (12%, 3%-32%)
	44-45 weeks	20/30 (67%, 47%-83%)	5/30 (17%, 6%-35%)	5/30 (17%, 6%-35%)	0/30 (0%, 0%-12%)	0/30 (0%, 0%-12%)	10/30 (33%, 17%-53%)
Fever ≥38°C	8-12 weeks	261/263 (99%, 97%-100%)	1/263 (0%, 0%-2%)	1/263 (0%, 0%-2%)	0/263 (0%, 0%-1%)	0/263 (0%, 0%-1%)	2/263 (1%, 0%-3%)
	15-25 weeks	22/23 (96%, 78%-100%)	0/23 (0%, 0%-15%)	0/23 (0%, 0%-22%)	1/23 (4%, 0%-15%)	0/23 (0%, 0%-15%)	1/23 (4%, 0%-15%)
	44-45 weeks	27/28 (96%, 82%-100%)	1/28 (4%, 0%-18%)	0/28 (0%, 0%-12%)	0/28 (0%, 0%-12%)	0/28 (0%, 0%-12%)	1/28 (4%, 0%-18%)
Chills	8-12 weeks	252/267 (94%, 91%-97%)	12/267 (4%, 2%-8%)	3/267 (1%, 0%-3%)	0/267 (0%, 0%-1%)	0/267 (0%, 0%-1%)	15/267 (6%, 3%-9%)
	15-25 weeks	19/24 (79%, 58%-93%)	3/24 (12%, 3%-32%)	2/24 (8%, 1%-27%)	0/24 (0%, 0%-14%)	0/24 (0%, 0%-14%)	5/24 (21%, 7%-42%)
	44-45 weeks	18/30 (60%, 41%-77%)	11/30 (37%, 20%-56%)	1/30 (3%, 0%-17%)	0/30 (0%, 0%-12%)	0/30 (0%, 0%-12%)	12/30 (40%, 23%-59%)
Joint pain	8-12 weeks	230/267 (86%, 81%-90%)	30/267 (11%, 8%-16%)	7/267 (3%, 1%-5%)	0/267 (0%, 0%-1%)	0/267 (0%, 0%-1%)	37/267 (14%, 10%-19%)
	15-25 weeks	21/24 (88%, 68%-97%)	3/24 (12%, 3%-32%)	0/24 (0%, 0%-14%)	0/24 (0%, 0%-14%)	0/24 (0%, 0%-14%)	3/24 (12%, 3%-32%)
	44-45 weeks	22/30 (73%, 54%-88%)	6/30 (20%, 8%-39%)	2/30 (7%, 1%-22%)	0/30 (0%, 0%-12%)	0/30 (0%, 0%-12%)	8/30 (27%, 12%-46%)
Muscle ache	8-12 weeks	193/267 (72%, 67%-78%)	64/267 (24%, 19%-30%)	10/267 (4%, 2%-7%)	0/267 (0%, 0%-1%)	0/267 (0%, 0%-1%)	74/267 (28%, 22%-33%)
	15-25 weeks	14/24 (58%, 37%-78%)	9/24 (38%, 19%-59%)	1/24 (4%, 0%-21%)	0/24 (0%, 0%-14%)	0/24 (0%, 0%-14%)	10/24 (42%, 22%-63%)
	44-45 weeks	14/30 (47%, 28%-66%)	11/30 (37%, 20%-56%)	5/30 (17%, 6%-35%)	0/30 (0%, 0%-12%)	0/30 (0%, 0%-12%)	16/30 (53%, 34%-72%)
Fatigue	8-12 weeks	141/267 (53%, 47%-59%)	86/267 (32%, 27%-38%)	38/267 (14%, 10%-19%)	2/267 (1%, 0%-3%)	0/267 (0%, 0%-1%)	126/267 (47%, 41%-53%)
	15-25 weeks	12/24 (50%, 29%-71%)	9/24 (38%, 19%-59%)	3/24 (12%, 3%-32%)	0/24 (0%, 0%-14%)	0/24 (0%, 0%-14%)	12/24 (50%, 29%-71%)
	44-45 weeks	9/30 (30%, 15%-49%)	15/30 (50%, 31%-69%)	6/30 (20%, 8%-39%)	0/30 (0%, 0%-12%)	0/30 (0%, 0%-12%)	21/30 (70%, 51%-85%)
Headache	8-12 weeks	142/267 (53%, 47%-59%)	103/267 (39%, 33%-45%)	22/267 (8%, 5%-12%)	0/267 (0%, 0%-1%)	0/267 (0%, 0%-1%)	125/267 (47%, 41%-53%)
	15-25 weeks	16/24 (67%, 45%-84%)	7/24 (29%, 13%-51%)	1/24 (4%, 0%-21%)	0/24 (0%, 0%-14%)	0/24 (0%, 0%-14%)	8/24 (33%, 16%-55%)

Symptom	V1-V2 Interval	None	Mild	Moderate	Severe	Potentially life threatening/ hospitalisation	Any
	44-45 weeks	9/30 (30%, 15%-49%)	17/30 (57%, 37%-75%)	3/30 (10%, 2%-27%)	1/30 (3%, 0%-17%)	0/30 (0%, 0%-12%)	21/30 (70%, 51%-85%)
Malaise	8-12 weeks	200/267 (75%, 69%-80%)	50/267 (19%, 14%-24%)	15/267 (6%, 3%-9%)	2/267 (1%, 0%-3%)	0/267 (0%, 0%-1%)	67/267 (25%, 20%-31%)
	15-25 weeks	18/24 (75%, 53%-90%)	4/24 (17%, 5%-37%)	2/24 (8%, 1%-27%)	0/24 (0%, 0%-14%)	0/24 (0%, 0%-14%)	6/24 (25%, 10%-47%)
	44-45 weeks	17/30 (57%, 37%-75%)	8/30 (27%, 12%-46%)	5/30 (17%, 6%-35%)	0/30 (0%, 0%-12%)	0/30 (0%, 0%-12%)	13/30 (43%, 25%-63%)
Nausea	8-12 weeks	234/267 (88%, 83%-91%)	27/267 (10%, 7%-14%)	4/267 (1%, 0%-4%)	2/267 (1%, 0%-3%)	0/267 (0%, 0%-1%)	33/267 (12%, 9%-17%)
	15-25 weeks	23/24 (96%, 79%-100%)	1/24 (4%, 0%-21%)	0/24 (0%, 0%-14%)	0/24 (0%, 0%-14%)	0/24 (0%, 0%-14%)	1/24 (4%, 0%-21%)
	44-45 weeks	25/30 (83%, 65%-94%)	4/30 (13%, 4%-31%)	1/30 (3%, 0%-17%)	0/30 (0%, 0%-12%)	0/30 (0%, 0%-12%)	5/30 (17%, 6%-35%)

Supplementary Table 5 - Overall summary of local and solicited adverse reactions in the first 7 days after each dose of vaccine for the two dose cohort

Interval group	Symptom	Dose	None	Any	Mild	Moderate	Severe	Moderate or severe	>2 moderate/severe symptoms
8-12 weeks	Any	1	4/267 (1%, 0%-4%)	263/267 (99%, 96%-100%)	149/267 (56%, 50%-62%)	95/267 (36%, 30%-42%)	19/267 (7%, 4%-11%)	114/267 (43%, 37%-49%)	63/267 (24%, 19%-29%)
		2	27/267 (10%, 7%-14%)	240/267 (90%, 86%-93%)	183/267 (69%, 63%-74%)	52/267 (19%, 15%-25%)	5/267 (2%, 1%-4%)	57/267 (21%, 17%-27%)	13/267 (5%, 3%-8%)
	Local	1	28/267 (10%, 7%-15%)	239/267 (90%, 85%-93%)	203/267 (76%, 70%-81%)	35/267 (13%, 9%-18%)	1/267 (0%, 0%-2%)	36/267 (13%, 10%-18%)	1/267 (0%, 0%-2%)
		2	66/267 (25%, 20%-30%)	201/267 (75%, 70%-80%)	195/267 (73%, 67%-78%)	6/267 (2%, 1%-5%)	0/267 (0%, 0%-1%)	6/267 (2%, 1%-5%)	0/267 (0%, 0%-1%)
	Systemic	1	33/267 (12%, 9%-17%)	234/267 (88%, 83%-91%)	127/267 (48%, 41%-54%)	88/267 (33%, 27%-39%)	19/267 (7%, 4%-11%)	107/267 (40%, 34%-46%)	57/267 (21%, 17%-27%)
		2	77/267 (29%, 23%-35%)	190/267 (71%, 65%-77%)	135/267 (51%, 44%-57%)	50/267 (19%, 14%-24%)	5/267 (2%, 1%-4%)	55/267 (21%, 16%-26%)	13/267 (5%, 3%-8%)
15-25 weeks	Any	1	2/24 (8%, 1%-27%)	22/24 (92%, 73%-99%)	11/24 (46%, 26%-67%)	8/24 (33%, 16%-55%)	3/24 (12%, 3%-32%)	11/24 (46%, 26%-67%)	5/24 (21%, 7%-42%)
		2	5/24 (21%, 7%-42%)	19/24 (79%, 58%-93%)	14/24 (58%, 37%-78%)	4/24 (17%, 5%-37%)	1/24 (4%, 0%-21%)	5/24 (21%, 7%-42%)	2/24 (8%, 1%-27%)
	Local	1	4/24 (17%, 5%-37%)	20/24 (83%, 63%-95%)	17/24 (71%, 49%-87%)	2/24 (8%, 1%-27%)	1/24 (4%, 0%-21%)	3/24 (12%, 3%-32%)	0/24 (0%, 0%-14%)
		2	9/24 (38%, 19%-59%)	15/24 (62%, 41%-81%)	12/24 (50%, 29%-71%)	3/24 (12%, 3%-32%)	0/24 (0%, 0%-14%)	3/24 (12%, 3%-32%)	0/24 (0%, 0%-14%)
	Systemic	1	3/24 (12%, 3%-32%)	21/24 (88%, 68%-97%)	10/24 (42%, 22%-63%)	9/24 (38%, 19%-59%)	2/24 (8%, 1%-27%)	11/24 (46%, 26%-67%)	3/24 (12%, 3%-32%)
		2	6/24 (25%, 10%-47%)	18/24 (75%, 53%-90%)	14/24 (58%, 37%-78%)	3/24 (12%, 3%-32%)	1/24 (4%, 0%-21%)	4/24 (17%, 5%-37%)	2/24 (8%, 1%-27%)
44-45 weeks	Any	1	0/30 (0%, 0%-12%)	30/30 (100%, 88%-100%)	6/30 (20%, 8%-39%)	17/30 (57%, 37%-75%)	7/30 (23%, 10%-42%)	24/30 (80%, 61%-92%)	13/30 (43%, 25%-63%)
		2	2/30 (7%, 1%-22%)	28/30 (93%, 78%-99%)	16/30 (53%, 34%-72%)	11/30 (37%, 20%-56%)	1/30 (3%, 0%-17%)	12/30 (40%, 23%-59%)	7/30 (23%, 10%-42%)
	Local	1	5/30 (17%, 6%-35%)	25/30 (83%, 65%-94%)	20/30 (67%, 47%-83%)	5/30 (17%, 6%-35%)	0/30 (0%, 0%-12%)	5/30 (17%, 6%-35%)	0/30 (0%, 0%-12%)
		2	7/30 (23%, 10%-42%)	23/30 (77%, 58%-90%)	19/30 (63%, 44%-80%)	4/30 (13%, 4%-31%)	0/30 (0%, 0%-12%)	4/30 (13%, 4%-31%)	0/30 (0%, 0%-12%)
	Systemic	1	1/30 (3%, 0%-17%)	29/30 (97%, 83%-100%)	6/30 (20%, 8%-39%)	16/30 (53%, 34%-72%)	7/30 (23%, 10%-42%)	23/30 (77%, 58%-90%)	12/30 (40%, 23%-59%)
		2	4/30 (13%, 4%-31%)	26/30 (87%, 69%-96%)	16/30 (53%, 34%-72%)	9/30 (30%, 15%-49%)	1/30 (3%, 0%-17%)	10/30 (33%, 17%-53%)	6/30 (20%, 8%-39%)

Supplementary Table 6 - Local and solicited adverse reactions in the first 7 days after vaccine for the third dose cohort

Symptom	Dose	None	Mild	Moderate	Severe	Potentially life threatening/ hospitalisation	Any
Pain	1	32/80 (40%, 29%-52%)	40/80 (50%, 39%-61%)	7/80 (9%, 4%-17%)	1/80 (1%, 0%-7%)	0/80 (0%, 0%-5%)	48/80 (60%, 48%-71%)
	2	10/15 (67%, 38%-88%)	5/15 (33%, 12%-62%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)	5/15 (33%, 12%-62%)
	3	40/80 (50%, 39%-61%)	32/80 (40%, 29%-52%)	8/80 (10%, 4%-19%)	0/80 (0%, 0%-5%)	0/80 (0%, 0%-5%)	40/80 (50%, 39%-61%)
Redness	1	77/80 (96%, 89%-99%)	2/80 (2%, 0%-9%)	1/80 (1%, 0%-7%)	0/80 (0%, 0%-5%)	0/80 (0%, 0%-5%)	3/80 (4%, 1%-11%)
	2	15/15 (100%, 78%-100%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)
	3	79/80 (99%, 93%-100%)	1/80 (1%, 0%-7%)	0/80 (0%, 0%-5%)	0/80 (0%, 0%-5%)	0/80 (0%, 0%-5%)	1/80 (1%, 0%-7%)
Warmth	1	69/80 (86%, 77%-93%)	10/80 (12%, 6%-22%)	1/80 (1%, 0%-7%)	0/80 (0%, 0%-5%)	0/80 (0%, 0%-5%)	11/80 (14%, 7%-23%)
	2	14/15 (93%, 68%-100%)	1/15 (7%, 0%-32%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)	1/15 (7%, 0%-32%)
	3	67/80 (84%, 74%-91%)	13/80 (16%, 9%-26%)	0/80 (0%, 0%-5%)	0/80 (0%, 0%-5%)	0/80 (0%, 0%-5%)	13/80 (16%, 9%-26%)
Itch	1	73/80 (91%, 83%-96%)	7/80 (9%, 4%-17%)	0/80 (0%, 0%-5%)	0/80 (0%, 0%-5%)	0/80 (0%, 0%-5%)	7/80 (9%, 4%-17%)
	2	14/15 (93%, 68%-100%)	1/15 (7%, 0%-32%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)	1/15 (7%, 0%-32%)
	3	73/80 (91%, 83%-96%)	7/80 (9%, 4%-17%)	0/80 (0%, 0%-5%)	0/80 (0%, 0%-5%)	0/80 (0%, 0%-5%)	7/80 (9%, 4%-17%)
Swelling	1	77/80 (96%, 89%-99%)	3/80 (4%, 1%-11%)	0/80 (0%, 0%-5%)	0/80 (0%, 0%-5%)	0/80 (0%, 0%-5%)	3/80 (4%, 1%-11%)

Symptom	Dose	None	Mild	Moderate	Severe	Potentially life threatening/ hospitalisation	Any
	2	15/15 (100%, 78%-100%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)
	3	79/80 (99%, 93%-100%)	1/80 (1%, 0%-7%)	0/80 (0%, 0%-5%)	0/80 (0%, 0%-5%)	0/80 (0%, 0%-5%)	1/80 (1%, 0%-7%)
Induration	1	78/80 (98%, 91%-100%)	1/80 (1%, 0%-7%)	1/80 (1%, 0%-7%)	0/80 (0%, 0%-5%)	0/80 (0%, 0%-5%)	2/80 (2%, 0%-9%)
	2	15/15 (100%, 78%-100%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)
	3	79/80 (99%, 93%-100%)	1/80 (1%, 0%-7%)	0/80 (0%, 0%-5%)	0/80 (0%, 0%-5%)	0/80 (0%, 0%-5%)	1/80 (1%, 0%-7%)
Tenderness	1	14/80 (18%, 10%-28%)	57/80 (71%, 60%-81%)	9/80 (11%, 5%-20%)	0/80 (0%, 0%-5%)	0/80 (0%, 0%-5%)	66/80 (82%, 72%-90%)
	2	6/15 (40%, 16%-68%)	9/15 (60%, 32%-84%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)	9/15 (60%, 32%-84%)
	3	20/80 (25%, 16%-36%)	54/80 (68%, 56%-78%)	6/80 (8%, 3%-16%)	0/80 (0%, 0%-5%)	0/80 (0%, 0%-5%)	60/80 (75%, 64%-84%)
Feverish	1	38/80 (48%, 36%-59%)	19/80 (24%, 15%-35%)	19/80 (24%, 15%-35%)	4/80 (5%, 1%-12%)	0/80 (0%, 0%-5%)	42/80 (52%, 41%-64%)
	2	13/15 (87%, 60%-98%)	1/15 (7%, 0%-32%)	0/15 (0%, 0%-22%)	1/15 (7%, 0%-32%)	0/15 (0%, 0%-22%)	2/15 (13%, 2%-40%)
	3	68/80 (85%, 75%-92%)	8/80 (10%, 4%-19%)	3/80 (4%, 1%-11%)	1/80 (1%, 0%-7%)	0/80 (0%, 0%-5%)	12/80 (15%, 8%-25%)
Fever $\geq 38^{\circ}\text{C}$	1	65/80 (81%, 71%-89%)	6/80 (8%, 3%-16%)	8/80 (10%, 4%-19%)	1/80 (1%, 0%-7%)	0/80 (0%, 0%-5%)	15/80 (19%, 11%-29%)
	2	15/15 (100%, 78%-100%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)
	3	76/77 (99%, 93%-100%)	1/77 (1%, 0%-7%)	0/77 (0%, 0%-5%)	0/77 (0%, 0%-5%)	0/77 (0%, 0%-5%)	1/77 (1%, 0%-7%)

Symptom	Dose	None	Mild	Moderate	Severe	Potentially life threatening/ hospitalisation	Any
Chills	1	38/80 (48%, 36%-59%)	21/80 (26%, 17%-37%)	18/80 (22%, 14%-33%)	3/80 (4%, 1%-11%)	0/80 (0%, 0%-5%)	42/80 (52%, 41%-64%)
	2	15/15 (100%, 78%-100%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)
	3	67/80 (84%, 74%-91%)	9/80 (11%, 5%-20%)	4/80 (5%, 1%-12%)	0/80 (0%, 0%-5%)	0/80 (0%, 0%-5%)	13/80 (16%, 9%-26%)
Joint pain	1	53/80 (66%, 55%-76%)	18/80 (22%, 14%-33%)	8/80 (10%, 4%-19%)	1/80 (1%, 0%-7%)	0/80 (0%, 0%-5%)	27/80 (34%, 24%-45%)
	2	15/15 (100%, 78%-100%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)
	3	71/80 (89%, 80%-95%)	8/80 (10%, 4%-19%)	1/80 (1%, 0%-7%)	0/80 (0%, 0%-5%)	0/80 (0%, 0%-5%)	9/80 (11%, 5%-20%)
Muscle ache	1	29/80 (36%, 26%-48%)	36/80 (45%, 34%-57%)	15/80 (19%, 11%-29%)	0/80 (0%, 0%-5%)	0/80 (0%, 0%-5%)	51/80 (64%, 52%-74%)
	2	13/15 (87%, 60%-98%)	2/15 (13%, 2%-40%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)	2/15 (13%, 2%-40%)
	3	53/80 (66%, 55%-76%)	24/80 (30%, 20%-41%)	3/80 (4%, 1%-11%)	0/80 (0%, 0%-5%)	0/80 (0%, 0%-5%)	27/80 (34%, 24%-45%)
Fatigue	1	16/80 (20%, 12%-30%)	36/80 (45%, 34%-57%)	26/80 (32%, 22%-44%)	2/80 (2%, 0%-9%)	0/80 (0%, 0%-5%)	64/80 (80%, 70%-88%)
	2	7/15 (47%, 21%-73%)	5/15 (33%, 12%-62%)	2/15 (13%, 2%-40%)	1/15 (7%, 0%-32%)	0/15 (0%, 0%-22%)	8/15 (53%, 27%-79%)
	3	37/80 (46%, 35%-58%)	31/80 (39%, 28%-50%)	11/80 (14%, 7%-23%)	1/80 (1%, 0%-7%)	0/80 (0%, 0%-5%)	43/80 (54%, 42%-65%)
Headache	1	19/80 (24%, 15%-35%)	32/80 (40%, 29%-52%)	23/80 (29%, 19%-40%)	6/80 (8%, 3%-16%)	0/80 (0%, 0%-5%)	61/80 (76%, 65%-85%)
	2	7/15 (47%, 21%-73%)	5/15 (33%, 12%-62%)	3/15 (20%, 4%-48%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)	8/15 (53%, 27%-79%)

Symptom	Dose	None	Mild	Moderate	Severe	Potentially life threatening/hospitalisation	Any
Malaise	3	43/80 (54%, 42%-65%)	29/80 (36%, 26%-48%)	8/80 (10%, 4%-19%)	0/80 (0%, 0%-5%)	0/80 (0%, 0%-5%)	37/80 (46%, 35%-58%)
	1	27/80 (34%, 24%-45%)	27/80 (34%, 24%-45%)	22/80 (28%, 18%-39%)	4/80 (5%, 1%-12%)	0/80 (0%, 0%-5%)	53/80 (66%, 55%-76%)
	2	12/15 (80%, 52%-96%)	1/15 (7%, 0%-32%)	1/15 (7%, 0%-32%)	1/15 (7%, 0%-32%)	0/15 (0%, 0%-22%)	3/15 (20%, 4%-48%)
Nausea	3	54/80 (68%, 56%-78%)	22/80 (28%, 18%-39%)	3/80 (4%, 1%-11%)	1/80 (1%, 0%-7%)	0/80 (0%, 0%-5%)	26/80 (32%, 22%-44%)
	1	59/80 (74%, 63%-83%)	14/80 (18%, 10%-28%)	7/80 (9%, 4%-17%)	0/80 (0%, 0%-5%)	0/80 (0%, 0%-5%)	21/80 (26%, 17%-37%)
	2	12/15 (80%, 52%-96%)	1/15 (7%, 0%-32%)	1/15 (7%, 0%-32%)	1/15 (7%, 0%-32%)	0/15 (0%, 0%-22%)	3/15 (20%, 4%-48%)
	3	72/80 (90%, 81%-96%)	7/80 (9%, 4%-17%)	1/80 (1%, 0%-7%)	0/80 (0%, 0%-5%)	0/80 (0%, 0%-5%)	8/80 (10%, 4%-19%)

Supplementary Table 7 - Overall summary of local and solicited adverse reactions in the first 7 days after vaccine for the third dose cohort

Symptom	Dose	None	Any	Mild	Moderate	Severe	Moderate or severe	>2 moderate/severe symptoms
Any	1	2/80 (2%, 0%-9%)	78/80 (98%, 91%-100%)	29/80 (36%, 26%-48%)	37/80 (46%, 35%-58%)	12/80 (15%, 8%-25%)	49/80 (61%, 50%-72%)	28/80 (35%, 25%-46%)
	2	3/15 (20%, 4%-48%)	12/15 (80%, 52%-96%)	8/15 (53%, 27%-79%)	3/15 (20%, 4%-48%)	1/15 (7%, 0%-32%)	4/15 (27%, 8%-55%)	2/15 (13%, 2%-40%)
	3	7/80 (9%, 4%-17%)	73/80 (91%, 83%-96%)	52/80 (65%, 54%-75%)	20/80 (25%, 16%-36%)	1/80 (1%, 0%-7%)	21/80 (26%, 17%-37%)	7/80 (9%, 4%-17%)
Local	1	11/80 (14%, 7%-23%)	69/80 (86%, 77%-93%)	57/80 (71%, 60%-81%)	11/80 (14%, 7%-23%)	1/80 (1%, 0%-7%)	12/80 (15%, 8%-25%)	0/80 (0%, 0%-5%)
	2	5/15 (33%, 12%-62%)	10/15 (67%, 38%-88%)	10/15 (67%, 38%-88%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)	0/15 (0%, 0%-22%)
	3	15/80 (19%, 11%-29%)	65/80 (81%, 71%-89%)	56/80 (70%, 59%-80%)	9/80 (11%, 5%-20%)	0/80 (0%, 0%-5%)	9/80 (11%, 5%-20%)	0/80 (0%, 0%-5%)
Systemic	1	7/80 (9%, 4%-17%)	73/80 (91%, 83%-96%)	25/80 (31%, 21%-43%)	37/80 (46%, 35%-58%)	11/80 (14%, 7%-23%)	48/80 (60%, 48%-71%)	27/80 (34%, 24%-45%)
	2	5/15 (33%, 12%-62%)	10/15 (67%, 38%-88%)	6/15 (40%, 16%-68%)	3/15 (20%, 4%-48%)	1/15 (7%, 0%-32%)	4/15 (27%, 8%-55%)	2/15 (13%, 2%-40%)
	3	18/80 (22%, 14%-33%)	62/80 (78%, 67%-86%)	45/80 (56%, 45%-67%)	16/80 (20%, 12%-30%)	1/80 (1%, 0%-7%)	17/80 (21%, 13%-32%)	4/80 (5%, 1%-12%)

Supplementary Table 8 – Model estimated geometric mean antibody responses assessed by tIgG ELISA after a single dose, from regression analysis shown in Figure 2A

Days from V1	Geometric mean (95% CI)	Geometric mean ratio compared with day 28 (95% CI)	Adjusted* geometric mean ratio compared with day 28 (95% CI)
28	198.5 (194.3, 202.9)	ref	ref
90	150.6 (140.5, 161.5)	0.76 (0.72, 0.80)	0.76 (0.72, 0.79)
180	100.9 (87.82, 116.0)	0.51 (0.45, 0.57)	0.50 (0.45, 0.57)
320	54.13 (42.27, 69.32)	0.27 (0.22, 0.34)	0.27 (0.21, 0.34)

*adjusted for age at enrolment

Supplementary Table 9 – Model estimated geometric mean T-cell responses assessed by IFN γ ELISpot after a single dose, from regression analysis shown in Figure 2B

Days from V1	Geometric mean (95% CI)	Geometric mean ratio compared with day 28 (95% CI)	Adjusted* geometric mean ratio compared with day 28 (95% CI)
28	490.4 (473.8, 507.4)	ref	ref
90	369.0 (330.5, 411.9)	0.75 (0.70, 0.81)	0.75 (0.70, 0.81)
180	244.2 (195.9, 304.3)	0.50 (0.41, 0.60)	0.50 (0.41, 0.60)

*adjusted for age at enrollment (age variable statistically insignificant, p=0.8990)

Supplementary Table 10 – Antibody responses assessed by tIgG ELISA after 2 doses.

P values shown for Kruskal-Wallis test when comparing three groups and Wilcoxon rank sum test with continuity correction when comparing two groups.

*adjusted for age at enrolment

Time-point	V1-V2 interval	n	Median [IQR]	Range	GMT (95% CI)	GMR (95% CI)	<i>P</i> value	Adjusted* GMT (95% CI)	Adjusted* GMR (95% CI)	<i>P</i> value*
V1	8-12 weeks	112	1 [1, 2]	1 - 290	2 (1, 2)					
	15-25 weeks	116	1 [1, 4]	1 - 916	2 (2, 3)					
	44-45 weeks	30	1 [1, 1]	1 - 267	2 (1, 3)					
V1+28	8-12 weeks	113	215 [124, 505]	1 - 5471	236 (185, 300)					
	15-25 weeks	115	184 [122, 393]	13 - 7092	245 (195, 309)					
	44-45 weeks	30	183 [138, 369]	35 - 3289	217 (150, 312)					
V1+56	44-45 weeks	29	119 [75, 216]	1 - 504	94 (54, 163)					
V1+182	44-45 weeks	30	112 [67, 147]	16 - 439	100 (74, 135)					
V2	8-12 weeks	115	161 [97, 376]	1 - 2524	173 (142, 212)					
	15-25 weeks	114	123 [74, 255]	4 - 1865	138 (112, 171)					
	44-45 weeks	30	76 [41, 109]	6 - 291	66 (48, 91)					
V2+28	8-12 weeks	113	923 [525, 1764]	1 - 4699	919 (756, 1117)	ref	<0.0001	931 (756, 1147)	ref	<0.0001
	15-25 weeks	108	1860 [917, 4992]	109 - 38065	1986 (1578, 2499)	2.16 (1.60, 2.92)		1969 (1592, 2434)	2.11 (1.57, 2.85)	
	44-45 weeks	30	3738 [1824, 6625]	348 - 46683	3982 (2703, 5864)	4.33 (2.82, 6.66)		3909 (2613, 5849)	4.20 (2.66, 6.62)	
V2+90	8-12 weeks	54	493 [213, 995]	76 - 2726	469 (360, 611)					
	15-25 weeks	79	1784 [649, 3811]	53 - 18067	1534 (1157, 2034)					
V2+182	8-12 weeks	62	278 [166, 499]	38 - 1715	307 (248, 380)	ref	<0.0001	306.3 (237, 395)	ref	<0.0001
	15-25 weeks	64	1280 [458, 2009]	45 - 15558	1034 (779, 1372)	3.37 (2.37, 4.79)		1036 (805, 1331)	3.38 (2.36, 4.85)	

Supplementary Table 11 - Antibody responses to SARS-CoV-2 Spike (Victoria strain) and Spike of other variants assessed by multiplex MSD assay in participants receiving 2 doses 44-46 weeks apart.

Antigen	Time Point	n	Median [IQR]	Range	GMT (95% CI)	n paired*	P value*
SARS-CoV-2 Spike (Victoria)	V1+28	29	7093 [4297, 17236]	1579 - 86914	8752 (5827, 13144)		
	V2	29	2167 [1211, 3522]	473 - 19566	2078 (1532, 2820)		
	V2+28	29	116758 [70316, 160414]	12111 - 420027	106929 (78743, 145206)	29	< 0.0001
D614G Spike	V1+28	29	7106 [4672, 14668]	1355 - 99692	9012 (5976, 13591)		
	V2	29	2697 [1812, 3647]	448 - 24893	2516 (1861, 3402)		
	V2+28	29	111967 [67682, 149049]	11497 - 417632	101452 (74723, 137743)	29	< 0.0001
B.1.1.7 Spike (alpha)	V1+28	29	5651 [3283, 12191]	765 - 62051	6034 (4044, 9004)		
	V2	29	1539 [1134, 2245]	161 - 5418	1478 (1102, 1982)		
	V2+28	29	81600 [49757, 119309]	6902 - 327702	75020 (54795, 102710)	29	< 0.0001
P.1 Spike (gamma)	V1+28	29	4062 [2512, 8059]	562 - 56681	4484 (2936, 6848)		
	V2	29	1298 [574, 2098]	130 - 5917	1131 (803, 1594)		
	V2+28	29	71093 [44260, 160209]	7234 - 260694	63376 (46638, 86122)	29	< 0.0001
B.1.351 Spike (beta)	V1+28	29	3073 [2190, 6373]	690 - 45433	3868 (2580, 5798)		
	V2	29	1111 [713, 1848]	103 - 3196	1067 (781, 1456)		
	V2+28	29	50315 [29210, 76079]	3831 - 182596	45478 (33061, 62558)	29	< 0.0001

*Statistics from Wilcoxon signed rank tests using V2 as the reference time-point

Supplementary Table 12 - Antibody responses assessed by tIgG ELISA in participants receiving 3 doses.

Time-point	V1-V2 interval	n	Median [IQR]	Range	GMT (95% CI)	n paired†	P value†
V1	8-16 weeks	75	2 [1, 5]	1 - 52	2 (2, 3)		
V1+28	8-16 weeks	74	192 [126, 504]	8 - 7092	254 (191, 337)		
V2	8-16 weeks	73	180 [84, 454]	4 - 1865	187 (141, 247)		
V2+28	8-16 weeks	73	1792 [899, 4634]	128 - 38065	1926 (1465, 2534)	73	ref
V3	8-16 weeks	75	555 [243, 1172]	36 - 6736	543 (419, 704)		
V3+14	8-16 weeks	74	2225 [1237, 4292]	47 - 7952	2007 (1615, 2494)		
V3+28	8-16 weeks	73	3746 [2047, 6420]	256 - 15865	3495 (2833, 4312)	73	0.0043

† Statistics from Wilcoxon signed rank tests using V2+28 as the reference time-point

Supplementary Table 13 - Antibody response to Beta variant (B.1.351) as assessed by tIgG ELISA in participants receiving 2 doses 44-46 weeks apart or 3 doses

Regimen	Time Point	n	Median [IQR]	Range	GMT (95% CI)	n paired*	P value*	n paired†	P value†
2 doses 44-46 weeks apart	V1+28	29	201 [129 – 448]	41 – 1747	233 (160, 339)			29	< 0.0001
	V2	30	105 [63 – 163]	1 – 322	79 (51, 122)				
	V2+28	30	3364 [2330 -5802]	152 - 21798	3429 (2316, 5078)				ref
3 doses	V2	45	122 [68 – 235]	13 - 962	118 (89, 156)				
	V2+28	45	1427 [680 – 2673]	114 – 18418	1407 (983, 2013)				ref
	V3	45	233 [129 – 611]	26 – 1983	268 (195, 368)		ref		
	V3+28	45	2016 [1009 – 3319]	55 - 15433	1794 (1341, 2401)	45	< 0.0001	45	0.2669

*Statistics from Wilcoxon signed rank tests using V3 as the reference time-point

† Statistics from Wilcoxon signed rank tests using V2+28 as the reference time-point

Supplementary Table 14 – Neutralising antibody responses to three VoCs in participants receiving 3 doses.

P values shown for pairwise comparisons using Wilcoxon sign rank test using V2+28 as the reference time-point

Time-point	Variant	n	Median [IQR]	Range	GMT (95% CI)	n paired	<i>P</i> value
V2+28	B.1.1.7 / Alpha	45	319 [176, 591]	20 - 3503	279 (200, 389)		
V3+28	B.1.1.7 / Alpha	42	612 [351, 920]	77 - 2606	545 (426, 698)	42	0.0023
V2+28	B.1.351 / Beta	45	54 [10, 113]	10 - 601	43 (30, 61)		
V3+28	B.1.351 / Beta	41	184 [66, 312]	10 - 1189	118 (78, 179)	41	< 0.0001
V2+28	B.1.617.2 / Delta	45	97 [38, 135]	10 - 1130	78 (55, 110)		
V3+28	B.1.617.2 / Delta	41	221 [110 – 471]	10 - 1496	206 (149, 284)	41	< 0.0001

Supplementary Table 15 - IFN- γ ELISpot response to peptides spanning the SARS-CoV-2 spike vaccine insert in participants receiving three doses of ChAdOx1 nCov-19.

Time-point	n	Median [IQR]	Range	GMT (95% CI)	n paired	GMR (95% CI)	<i>P</i> value *	n paired	GMR (95% CI)	<i>P</i> value†
V2+14	14	347 [200, 894]	2948 - 14	393 (221, 697)						
V2+28	15	475 [307, 1087]	1343 - 15	452 (272, 749)				-	ref	-
V3	15	200 [127, 389]	993 - 15	235 (149, 369)	-	ref	-			
V3+14	15	264 [131, 452]	1060 - 15	255 (155, 420)	15	1.09 (0.78, 1.51)	0.5701			
V3+28	12	399 [314, 662]	1826 - 12	442 (296, 659)	12	1.73 (1.23, 2.43)	0.0121	12	0.79 (0.63, 1.00)	0.0597

*Statistics from Wilcoxon signed rank tests using V3 as the reference time-point

† Statistics from Wilcoxon signed rank tests using V2+28 as the reference time-point

Supplementary References

1. Ramasamy MN, Minassian AM, Ewer KJ, et al. Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): a single-blind, randomised, controlled, phase 2/3 trial. *Lancet* 2021; **396**(10267): 1979-93.

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